

422 Rec'd PCT/PTO 22 MAR 2000

CLAIM

1. A method, for preparing a natural humanized antibody, which comprises conducting a homology search for the FR of a primary design antibody and selecting a natural human FR retaining the artificial amino acid residues contained in the FR of the primary design antibody and having a homology therewith.

2. The method of preparing a natural humanized antibody according to claim 1, which comprises conducting a homology search for the FR of a primary design antibody, selecting a natural human FR retaining the artificial amino acid residues contained in the FR of the primary design antibody and having a homology therewith, and replacing one or a plurality of different amino acid residues between the FR of the primary design antibody and the selected natural human FR.

20 ~~3. The method of preparation according to claim 1 or 2, wherein the primary design antibody comprises CDRs derived from a first animal species, and FRs derived from a second animal species and having artificial amino acid residues.~~

4. The method of preparation according to claim 3, wherein the first animal species is rat and the second animal species is human.

25 ^{Sub} 5. The method of preparation according to ^{Claim 1} ~~any of~~
~~claims 1 to 4~~, wherein the artificial amino acid residues
are derived from the PR of non-human antibody.

6. A natural humanized antibody obtained by a method of preparation according to, ~~any of the claims 1 to~~ ^{claim 1}

7. A natural humanized antibody containing CDR derived from a first animal species and the FR derived from a second animal species, characterized in that said FR comprises an amino acid sequence having amino acid residue different from the FR used for CDR-grafting by one or a plurality of amino acid residues and that said FR has been replaced with an FR derived from a second

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9. DNA encoding the natural humanized antibody according to ~~any of claims 6 to 8.~~ ^{claim 6}

10 11. A host comprising the DNA according to claim
10.

12. A method of preparing a natural humanized antibody, which comprises culturing the cells into which an expression vector comprising the DNA according to claim 9 has been introduced and recovering the desired natural humanized antibody from the culture of said cells.

13. A pharmaceutical composition comprising a natural humanized antibody.

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